IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	SHEN et al.
Application No.:	10/646,664
For:	METHODS OF DIRECTING C-O BOND FORMATION UTILIZING A TYPE II POLYKETIDE SYNTHASE SYSTEM
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AMENDMENT AND RESPONSE

In response to the Office Action dated January 19, 2006, please amend the above-identified application as indicated below.

Amendments to the Claims are reflected in the Listing of Claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 8 of this paper.

Listing of Claims:

The Listing of Claims set forth below shall replace all prior versions and listings of claims in the application.

1. (Original) A method of modifying a biological molecule by formation of a C-O bond, comprising the steps of contacting a biological molecule which is a substrate for a polypeptide selected from the group consisting of:

(a) a polypeptide comprised by an amino acid sequence set forth in SEQ ID NO. 3;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 2; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 2 and capable of C-O bond formation;

with said polypeptide whereby said polypeptide modifies the biological molecule by formation of a C-O bond.

2. (Original) A method according to claim 1 further comprising the step of contacting the biological molecule modified by the polypeptide recited in claim 1 with a second polypeptide selected from the group consisting of:

(a) a polypeptide comprised by an amino acid sequence set forth in SEQ ID NO. 5;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 4; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 4 and capable of C-O bond formation;

whereby said second polypeptide further modifies the biological molecule by formation of a C-O bond.

3. (Original) A method according to claim 1 wherein the C-O bond formed is between the biological molecule and a second biological molecule, said second biological molecule also a substrate for the polypeptide.

4. (Original) A method according to claim 1 wherein said contacting is in a host cell.

5. (Original) A method according to claim 4 wherein said host cell is a bacterium.

6. (Original) A method according to claim 4 where the host cell is a eukaryotic cell selected from the group consisting of a mammalian cell, a yeast cell, a plant cell, a fungal cell, and an insect cell.

7. (Original) A method according to claim 4 wherein said biological molecule is an exogenously supplied substrate.

8. (Original) A method according to claim 1 wherein the contacting is *ex vivo*.

9. (Original) A method according to claim 1 wherein said method produces a macrotetralide or a macrotetralide analogue.

10. (Original) A method of catalyzing a C-O bond between biological molecules, comprising the steps of contacting biological molecules which are substrates for at least one polypeptide capable of catalyzing C-O bond formation between said biological molecules and encoded by a nucleic acid set forth in SEQ ID NO. 1 or a nucleic acid hybridizing under stringent conditions thereto, with said polypeptide whereby said polypeptide catalyzes C-O bond formation between the biological molecules.

11. (Original) A method according to claim 10 wherein said contacting is in a host cell.

12. (Original) A method according to claim 11 wherein said host cell is a bacterium.

13. (Original) A method according to claim 11 wherein said host cell is a eukaryotic cell

selected from the group consisting of a mammalian cell, a yeast cell, a plant cell, a fungal cell, and an insect cell.

14. (Original) A method according to claim 11 wherein at least one of said biological molecules is an exogenously supplied substrate.

15. (Original) A method according to claim 10 wherein the contacting is *ex vivo*.

16. (Original) A method according to claim 10 wherein said method produces a macrotetralide or a macrotetralide analogue.

17. (Original) A method of producing a macrotetralide or a macrotetralide analogue, comprising the steps of contacting biological molecules that are substrates for at least one polypeptide selected from the group consisting of:

(a) a polypeptide encoded by an amino acid sequence set forth in SEQ ID NO. 3 or 5;

(b) a polypeptide encoded by a nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO. 2 or 4; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 2 or 4 and capable of C-O bond formation;

with said polypeptide under conditions such that the polypeptide catalyzes a C-O bond between the biological molecules and a macrotetralide or macrotetralide analogue is thereby synthesized; and

recovering said macrotetralide or macrotetralide analogue.

18. (Original) A method according to claim 17 wherein said method is carried out in a host cell and at least one biological molecule is an exogenously supplied substrate.

19. (Withdrawn) A method of preparing a hybrid enzyme comprising the step of positioning in a hybrid enzyme at least one catalytic domain capable of catalyzing C-O bond formation between biological molecules, said catalytic domain encoded by a polypeptide selected from the group consisting of:

(a) a polypeptide encoded by an amino acid sequence set forth in SEQ ID NO. 3 or 5;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 2 or 4;

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 2 or 4 and capable of C-O bond formation.

20. (Withdrawn) A method of preparing a megasynthetase comprising the step of positioning in a megasynthetase at least one module including a polypeptide capable of catalyzing C-O bond formation between biological molecules, said polypeptide selected from the group consisting of:

(a) a polypeptide encoded by an amino acid sequence set forth in SEQ ID NO. 3 or 5;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 2 or 4; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 2 or 4 and capable of C-O bond formation.

21. (Original) A method of catalyzing C-O bond formation between biological molecules, comprising steps of contacting biological molecules that are substrates for a polypeptide selected from the group consisting of:

(a) a polypeptide comprised by an amino acid sequence set forth in SEQ ID NO. 3;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 2; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 2 and capable of C-O bond formation;

with said polypeptide whereby said polypeptide catalyzes C-O bond formation between the biological molecules.

22. (Original) A method according to claim 21 wherein said method is performed in a host cell and at least one of the biological molecules is an exogenously supplied substrate.

23. (Original) A method of catalyzing C-O bond formation between biological molecules, comprising steps of contacting biological molecules that are substrates for a polypeptide selected from the group consisting of:

(a) a polypeptide comprised by an amino acid sequence set forth in SEQ ID NO. 5;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence set forth in SEQ ID NO. 4; and

(c) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 4 and capable of C-O bond formation;

with said polypeptide whereby said polypeptide catalyzes C-O bond formation between the biological molecules.

24. (Original) A method according to claim 23 wherein said method is performed in a host cell and at least one of the biological molecules is an exogenously supplied substrate.

25. (Original) A method of chemically modifying a biological molecule by formation of a C-O bond, comprising contacting a biological molecule that is a substrate for a polypeptide selected from the group consisting of:

(a) a polypeptide encoded by an amino acid sequence set forth in SEQ ID NO. 3 or 5;

(b) a polypeptide encoded by a nucleic acid comprising nucleotide sequence identical to or isolated from SEQ ID NO. 1, 2 or 4;

(c) a polypeptide encoded by a nucleic acid encoding an amino acid sequence set forth in SEQ ID NO. 3 or 5; and

(d) a polypeptide encoded by a nucleic acid that specifically hybridizes under stringent conditions to SEQ ID NO. 1, 2 or 4;

with said polypeptide whereby said polypeptide chemically modifies the biological molecule by formation of a C-O bond.

Remarks/Arguments

Status of claims:

All original claims in the application, namely claims 1-25 are currently pending. Of these claims, claims 19 and 20 are withdrawn from consideration, as shown in the listing of claims.

Arguments:

Responsive to the restriction requirement in the Office Action dated January 19, 2006, the claims of Group I (Claims 1-18 and 21-25, classified in class 530, subclass 350, class 536, subclass 23.2 and class 435, subclass 69.1) are elected for prosecution with traverse. Applicant reserves the right to file a continuing or divisional application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicant does not hereby abandon or waive any rights in the non-elected inventions.

Applicant respectfully traverses the restriction requirement, in particular the restriction of Groups I (Claims 1-18, 21-25), II (Claim 19) and III (Claim 20), all of which are classified in class 530, subclass 350, class 536, subclass 23.2 and class 435, subclass 69.1. The Action states these groups are patentably distinct from each other because they have different method steps, use different materials and produce different results. While these claims are patentably distinct, the classification of these groups into the same class and subclass argues for substantial similarities as well.

Thus, the classification of Group I, II and III into class 530, subclass 350, class 536, subclass 23.2 and class 435, subclass 69.1 indicates that searching Groups I, II and III would not be burdensome. Furthermore, since all these claims have common materials, namely SEQ ID. Nos. 2, 3, 4 and 5, a search for claims in Group I, namely Claims 1-18 and 21-25, having these sequences will inevitably result in coextensive searches for claims in Group II and III having the same set of nucleic acid/amino acid sequences. Accordingly, a search for non-elected group is not unduly burdensome. Applicant submits that the restriction of Groups I, II, and III is improper and should be withdrawn.

CONCLUSIONS

Applicant respectfully submits that claims 1-18 and 21-25 are in a condition for allowance and notice to that effect is earnestly solicited. Further, Applicant requests reconsideration of the restriction requirement such that claims 19 and 20 may be prosecuted along with claims of group I.

The Examiner is urged to telephone the undersigned in the event a telephone discussion would be helpful in advancing the prosecution of the present application. The Office is further authorized to charge the processing fee or any other surcharges, or underpayment, including extension of time, as deemed necessary and appropriate to the Deposit Account 07-1509 of Godfrey & Kahn, S.C.

Respectfully Submitted,

GODFREY & KAHN, S.C.

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